

Thus, it is emphasized that the statute (e.g., the first paragraph of 35 U.S.C. §112) does not forbid all experimentation, only undue experimentation. It is respectfully submitted that, as seen in the respective Declarations submitted with the Amendment filed January 27, 2005 and the Amendment filed September 11, 2003, and as is clear from the guidance provided in Applicants' specification, sufficient guidance is provided to one of ordinary skill in the art to practice the present invention, without undue experimentation.

Initially, attention is respectfully directed to Applicants' specification, and in particular Examples 1-3 on pages 8-11 thereof. It is respectfully submitted that the Examples show techniques according to the present invention, both for culturing a microorganism belonging to *Escherichia coli*, having an ability to produce L-histidine and having resistance to 150 mg/l primaquine or the alkali metal salts thereof, as in claim 1, or for culturing a mutant strain having an increased resistant to primaquine or alkali metals salts thereof, as in claim 13, providing guidance to one of ordinary skill in the art to make and use the present invention.

As seen in the respective Declarations of Tetsuya Abe submitted with the amendment of September 11, 2003 and January 27, 2005, it is respectfully submitted that merely routine experimentation is required for practicing the methods as in claims 1 and 13, such that the quantity of experimentation is not undue. Note Manual of Patenting Examining Procedure 2164.06.

In particular, it is respectfully submitted that, in order to determine whether a specific microorganism belonging to *Escherichia coli* can be used as in the present claims being considered on the merits, one of ordinary skill in the art need only

culture the microorganism, produce and accumulate L-histidine in the culture medium therefrom and recover L-histidine (see claim 1); or culture a mutant strain obtained by mutagenizing a microorganism belonging to *Escherichia coli* and having an ability to produce L-histidine, producing and accumulating and then recovering the L-histidine. It is respectfully submitted that such processing, for determining whether a specific microorganism belonging to *Escherichia coli* produced and accumulated L-histidine, recoverable from the culture medium, would not constitute undue experimentation. See In re Angstadt, 190 USPQ 214 (CCPA 1976).

Moreover, it is emphasized that, under the present facts, the Examiner has merely alleged that the specification is not enabling to show or suggest that resistance to the specified amount of primaquine is a measuring stick for an *Escherichia coli* that accumulates amounts of L-histidine in a culture medium, as claimed. However, it is respectfully submitted that Applicants' specification as originally filed describes the production of, e.g., L-histidine, and recovery thereof, by culturing a specific microorganism belonging to *Escherichia coli*, having resistance to 150 mg/l primaquine (note, for example, Example 1 on pages 8 and 9 of Applicants' specification), and also provides a general description of culturing other microorganisms belonging to *Escherichia coli* having resistance to 150 mg/l primaquine, and producing, accumulating and recovering L-histidine. It is respectfully submitted that the Examiner has not satisfied his burden of establishing a reasonable basis to question the enablement provided for the presently claimed invention. Note Manual of Patent Examining Procedure 2164.04. See also In re Dinh-Nguyen, 181 USPQ 46 (CCPA 1974); and In re Bowen, 181 USPQ 48 (CCPA

1974). Since the Examiner has not even satisfied the initial burden questioning the enablement provided in Applicants' specification, clearly the rejection under the first paragraph of 35 U.S.C. §112, as set forth in the Office Action mailed March 11, 2005, is improper.

The comment by the Examiner in the second paragraph on page 2 of the Office Action mailed March 11, 2005, that Table 1 on page 5 of the Declaration submitted January 27, 2005 indicates that the strain TZA-51 "does not produce L-histidine", is respectfully traversed. Thus, as can be seen in Table 1 on page 5 of the Declaration submitted with the Amendment on January 27, 2005, the bacterial strain or TZA-51 produced 0.16 g/l of L-histidine. This Table 1 on page 5 of the Declaration submitted January 27, 2005, shows that the strains formed by mutagenesis from this TZA-51 strain, each having more resistance to primaquine disodium salt, than the TZA-51 strain, produced more L-histidine than the TZA-51 strain. Specifically, it is respectfully submitted that the Examiner errs in construing this Declaration submitted with the Amendment of January 27, 2005, as indicating that the strain TZA-51 does not produce L-histidine.

The further contention by the Examiner in the last paragraph on page 2 of the Office Action mailed March 11, 2005, that the effect of resistant to 400 mg/l primaquine "is not informative" to demonstrate a clear correlation between resistance to 150 mg/l primaquine and the production of L-histidine by any *E. coli*, is respectfully traversed. It is respectfully submitted that one of ordinary skill in the art would have known that the strains TPQ-1, TPQ-3, TPQ-8 and TPQ 11, shown in the Declaration submitted January 27, 2005, obtained by picking up large colonies

appearing on an agar plate containing 400 mg/l primaquine disodium salt, would also make large colonies on an agar plate containing that the primaquine compound at a concentration of less than 400 mg/l. That is, these strains, having a resistance to 400 mg/l, would also have resistance to 150mg/l primaquine disodium salt.

It is respectfully submitted that the preparation of microorganisms having resistance to 400 mg/l primaquine disodium salt is a means to obtain microorganisms having resistance to 150 mg/l primaquine disodium salt.

Moreover, it is respectfully submitted that the Declarations of T. Abe, respectively submitted January 27, 2005, and September 11, 2003, establish that further strains having properties recited in the claims can be obtained without undue experimentation; and that, accordingly, establish that the presently claimed method can be, e.g., used without undue experimentation.

In view of all the foregoing, it is respectfully submitted that the Examiner has not satisfied his initial burden under the enablement requirement, of establishing that one of ordinary skill in the art could not practice the presently claimed invention without undue experimentation.

However, even assuming, arguendo, that the Examiner has established a prima facie case of lack of enablement, Applicants, through all the evidence of record, including guidance provided in their specification and examples provided therein, and the two Declarations submitted respectively on September 11, 2003 and January 27, 2005, clearly overcome such prima facie case and shift the burden back to the Examiner, and the Examiner has provided no evidence establishing lack of enablement. In view of all the foregoing, entry of the present Request for

Reconsideration, and reconsideration and allowance of claims 1 and 13, in addition to claim 5, in due course, are respectfully requested.

Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, or credit any overpayment of fees, to the deposit account of Antonelli, Terry, Stout & Kraus, LLP, Deposit Account No. 01-2135 (referencing case no. 506.39084X00).

Respectfully submitted,

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A handwritten signature in black ink, appearing to read "William I. Solomon", with a long horizontal flourish extending to the right.

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